Real-time contrast enhanced ultrasound-guided percutaneous biopsy in diagnosing gallbladder carcinoma metastasising to the ovaries: a case report

Jing Wang
The First Affiliated Hospital of China Medical University

Yanjun Liu (lyj7512cmu@163.com)
The First Affiliated Hospital of China Medical University

Liang Sang
The First Affiliated Hospital of China Medical University

Weina Wan
The First Affiliated Hospital of China Medical University

Case Report

Keywords: CEUS, percutaneous biopsy, gallbladder carcinoma, krukenberg tumor

Posted Date: February 7th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2543650/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Introduction: Multiple-organ primary tumors can invade the ovary through lymphatic and hematogenous routes presenting as ovarian Krukenberg tumors (KT); however, they rarely originate from the gallbladder and are often present as primary ovarian tumors; however, their treatments are totally different.

Patient concerns: A 62-year-old Chinese woman presented with abdominal distension for six months and a weight loss of 5 kg for two months.

Diagnoses: Based on multiple imaging examinations, the patient was preliminarily diagnosed with a malignant tumor of unknown origin with multiple metastases (liver, gallbladder, right-adnexal, omentum). To identify the origin of the malignancy, the patient received real-time contrast enhanced ultrasound-guided (CEUS-guided) percutaneous biopsy. The postsurgical pathologic examination showed perihepatic hypoecho and right-adnexal mass were both metastatic adenocarcinoma from the gallbladder.

Interventions: The patient received chemotherapy with gemcitabine and cisplatin instead of surgery; however, after six cycles, the lesion increased after reexamination, so the treatment was changed to combination with duvariumab regimen for 5 cycles.

Outcomes: At present, the treatment process went smoothly with no recurrence or obvious progress during follow-up.

Conclusions: Differential diagnosis between primary and metastatic ovarian tumors is important. Early diagnosis and effective treatment options are essential for patient survival. The punch biopsy is significant for patients with multiple metastases that cannot tolerate surgery.

Ethical compliance: All procedures performed in studies involving human participants comply with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki Declaration and its later amendments or similar ethical standards.

Data Access Statement: The research data supporting this publication is available from the NN repository at www.NNN.org/download/

Introduction

The krukenberg tumor is a rare metastatic ovarian malignancy, and the most tumors originate from the gastrointestinal tract, such as stomach, and colon. However, cases originating from gallbladder or hepatic bile duct are little known[1]. These metastatic tumors are usually bilateral; few cases can be seen unilaterally[2]. We reported a rare case that presents as an metastatic right-ovarian malignancy of gallbladder origin and share our analysis of imaging findings, diagnosis, and treatment methods.

Case Presentation
A 62-year-old Chinese woman presented with abdominal distension for six months and weight loss of 5 kg for two months. The patient had a history of hypertension, coronary disease, and diabetes but she denied any abnormal vaginal discharge or bleeding. Her physical examination showed an immobile egg-sized mass with pressing pain located right posterior to the uterus. Laboratory tests showed the patient's level of carbohydrate antigen 125 (CA125) was 135.00 U/mL, CA199 was 651.00 U/mL, CA724 was 10.30 U/mL, all of these were higher than the normal level.

Gynecologic ultrasonography (Fig. 1) described an irregularly substantial mass sized 4.4×3.8 cm with rich blood flow in the right accessory area. Abdominal ultrasonography showed the gallbladder wall is thickening and partially indistinct, and also showed an uneven hypoecho sized 3.3×2.5 cm in the gallbladder cavity. Liver tissue adjacent the gallbladder displayed irregularly hypoecho.

Enhanced abdominal computed tomography (CT) examination showed the gallbladder wall is thickening and irregular with malignant change inside, and adjacent liver tissue is involved. The right adnexal area showed an uneven enhancement mass which diagnosed as suspicious for malignancy. In addition, it also showed fluid density in the abdominal and pelvic cavities. Positron emission tomography-computed tomography (PET-CT) examination was performed for further evaluation, which showed metabolic enhancements not only in the right ovarian mass, gallbladder and hepatic tissue but also in omentum, intestinal canal, abdomen and pelvic cavity (Fig. 2).

The patient received Multi-Disciplinary Treatment (MDT), according to these examination results, the patient was preliminarily diagnosed with malignant tumor of unknown origin with multiple metastases. To identify the origin of the malignancy, the patient received real-time contrast enhanced ultrasound-guided (CEUS-guided) percutaneous biopsy. The postsurgical pathologic examination showed perihepatic hypoecho and right-adnexal mass were both metastatic adenocarcinoma from the gallbladder (Fig. 3). Immunohistologic tests showed positive expression of caudal type homeobox 2 (CDX2), cytokeratin 7 (CK7), cytokeratin 20 (CK20), Ki-67 (60%+), and negative expression of SATB2 and pair box gene 8 (PAX8) (Fig. 4).

Considering that our patient had multiple metastatic lesions and accompanied by basic diseases such as hypertension, coronary disease, and diabetes, she received a chemotherapy with gemcitabine and cisplatin instead of surgery. But the outcome is poor. She was regularly followed up. After 6 cycles, the lesion increased after reexamination, so the treatment was changed to combination with duvariumab regimen for 5 cycles. At present, the treatment process went smoothly with no recurrence or obvious progress after follow-up.

Consent for publication

The patient provided a written informed consent to publish the case.

Discussion
Metastatic ovarian cancer often origins from various organs, represents about 5-15% of all ovarian tumors[3-5], krukenberg tumors is only 1-2% of them[6], which often confused with primary ovarian tumours and teratoma. Most patients with gallbladder-derived ovarian malignant tumors have no obvious and specific clinical manifestations, often manifested as abdominal pain or abdominal distension, and only a few patients can appear with gallbladder cancer-related symptoms, such as jaundice[7-8]. In our case, only abdominal distension was presented as the first symptom with the pelvic mass touched during physical examination. The patient also had insidious abdominal pain, but it is considered as gastritis. In addition, the ascites usually represents an advanced stage of cancer.

No clear differences between primary and metastatic ovarian tumors have been drawn from the current imaging reports[9]. However, imaging examination has certain diagnostic significance for ovarian metastatic tumors. First, imaging examination can detect lesions outside the accessory area, thus increasing the diagnosis of metastatic ovarian cancer. Preoperative US, CT, and PET-CT can evaluate the disease progression and provide guidance for treatment. Secondly, it has been reported that the metastatic ovarian cancer is usually bilateral and is more common on the right side[2]. Therefore, when bilateral tumors are found, other organs are often examined to determine the presence of a primary malignancy. In addition, metastatic ovarian cancer often presents as solid mass or mixed cystic mass, while primary ovarian tumor often presents as cystic mass or with liquefied necrosis area[10]. The imaging of our case showed a solid main mass, which is different from the primary ovarian cancer. While it appears as a unilateral ovarian mass, which increases the difficulty of diagnosis. The patient's imaging findings are useful for showing systemic metastasis, but specific characteristics are lacking. So we chose a real-time CEUS-guided needle biopsy to identify the primary lesion. Needle biopsy may be conclusive in such a clinical situation as the case in diagnosing.

Enhanced ultrasound can show tumor blood vessels and necrotic lesions clearly. We selected the contrast enhanced site for percutaneous needle biopsy to improve the positive rate[11-12]. At the same time, CEUS-guided percutaneous biopsy can monitor the position of the biopsy needle to avoid damaging tissue and blood vessels around the mass[13]. In our case, after injection of contrast media, the lesion began to strengthen earlier than the uterine muscle wall which showed uneven high enhancement. Large blood vessels were seen in the lesion entering the interior from the side of the mass. And weak enhanced area internally was seen and considered as necrotic or liquefaction. Therefore, during the puncture process, we avoided the central necrotic part and selected the enhancement area and obtained positive results.

Metastatic ovarian tumors are very difficult to distinguish from primary tumors. However, it is significant to distinguish between them because the corresponding treatments are quite different. Differential diagnosis often rely on patient's medical history and immunohistochemical examination. CK7 and CK20 are important markers for distinction in ovarian tumors[14]. CDX-2 is highly expressed in gallbladder cancer, while is negative in primary ovarian cancer. SATB2 is highly expressed in the lower epithelial tissues of the digestive tract. In addition, negative expression in Pax8 can clearly exclude the primary tumor and support the metastatic origin[15].
At present, there is no standard and consensus of the treatment method for metastatic ovarian cancer. For primary tumors, appropriate surgery may prolong survival, but it works little in metastatic ones which need combination with radiotherapy or chemotherapy regimen. In addition, primary ovarian tumors are commonly sensitive to platinum, while gallbladder cancer often requires a combination of gemcitabine[16]. However, the prognosis of our patient was extremely poor. After two courses of gemcitabine and platinum drugs, the mass was found to increase, and the tumor marker value increased. So we switched to combination with dovaliuzumab for 6 courses, the review results were shown to be effective.

**Conclusion**

The case we report is very rare. First, the metastatic tumors of the ovary are extremely rare primary to the gallbladder. Secondly, the metastatic ovarian cancer is usually bilateral while in our case, it showed unilateral metastasis, which increases the difficulty of diagnosis. The punch biopsy is significant for patients with multiple metastases that cannot tolerate surgery. Although a medical history and imaging examination can help to rule out primary ovarian cancer, the definitive diagnosis was still upon histopathologic examination.

**Declarations**

**Acknowledgements**

We sincerely appreciate the written consent of the patient.

**Funding**

This study was supported by the Scientific Research Project Foundation of Education Department of Liaoning Province of China (NO.FWZR2020005)

The authors have no conflicts of interest to disclose.

**References**


**Figures**
Figure 1

Ultrasound examination

A. CEUS showed that the gallbladder and intrahepatic hypoecho were enhanced earlier than other parts of the liver.

B. an irregularly substantial mass was seen in the right c area which showed uneven high enhancement with rapid advance and rapid exit in CEUS.
CT and PET-CT imaging

A. PET showed increased FDG uptake in the fossa for gallbladder and adjacent liver tissue with a maximum SUV of 8.2, CT showed enhancement of thickened gallbladder wall and low density in liver with underdefined boundaries.

B. PET showed an increased FDG uptake area in the right adnexal area with a maximum SUV of 5.8, and CT showed the soft tissue nodules.
Figure 3

Pathological image($\times$200).

The tumor cells were arranged in a glandular tubule pattern with invasive growth.

Figure 4
Immunohistochemical staining (×100).

A: CK7(+); B: CDX2(+); C: PAX8(-); D: SATB2(-)